Message

From: Olinger, Christine [Olinger.Christine@epa.gov]
Sent: 6/3/2019 5:12:44 PM
To: Wilbur, Donald [Wilbur.Donald@epa.gov]; Huskey, Angela [Huskey.Angela@epa.gov]; Ertman, AWillis [Ertman.AWillis@epa.gov]; Perron, Monique [Perron.Monique@epa.gov]
CC: Godshall, Joshua [Godshall.Joshua@epa.gov]; Fitz, Nancy [Fitz.Nancy@epa.gov]; Muhammad, Maryam K. [Muhammad.Maryam@epa.gov]; Davis, Kable [Davis.Kable@epa.gov]; Giles-Parker, Cynthia [Giles-Parker.Cynthia@epa.gov]; Davis, Donna [Davis.Donna@epa.gov]
Subject: RE: Cumulative language for Conazoles - Conversation with Angela Huskey - Mefentrifluconazole
Attachments: Triazole Aggregate with Mefen.docx

Forgot to attach the document that should be referenced in the FR.

From: Olinger, Christine
Sent: Monday, June 3, 2019 1:07 PM
To: Wilbur, Donald <Wilbur.Donald@epa.gov>; Huskey, Angela <Huskey.Angela@epa.gov>; Ertman, AWillis <Ertman.AWillis@epa.gov>; Perron, Monique <Perron.Monique@epa.gov>
Cc: Godshall, Joshua <Godshall.Joshua@epa.gov>; Fitz, Nancy <Fitz.Nancy@epa.gov>; Muhammad, Maryam K. <Muhammad.Maryam@epa.gov>; Davis, Kable <Davis.Kable@epa.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Davis, Donna <Davis.Donna@epa.gov>
Subject: RE: Cumulative language for Conazoles - Conversation with Angela Huskey - Mefentrifluconazole

Angela –
We did reference the conazole aggregate assessment in the final risk assessment.

Chris Olinger

Christine Olinger
Chief, Risk Assessment Branch I
Office of Pesticide Programs Health Effects Division
US Environmental Protection Agency
1200 Pennsylvania Ave NW MailCode 7509P
Washington DC 20460
Office Location: Potomac Yard South Room 10751
Phone: 703-305-5406
FAX: 703-305-5147
olinger.christine@epa.gov

From: Wilbur, Donald
Sent: Monday, June 3, 2019 1:05 PM
To: Huskey, Angela <Huskey.Angela@epa.gov>; Ertman, AWillis <Ertman.AWillis@epa.gov>; Perron, Monique <Perron.Monique@epa.gov>; Olinger, Christine <Olinger.Christine@epa.gov>
Cc: Godshall, Joshua <Godshall.Joshua@epa.gov>; Fitz, Nancy <Fitz.Nancy@epa.gov>; Muhammad, Maryam K. <Muhammad.Maryam@epa.gov>; Davis, Kable <Davis.Kable@epa.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Davis, Donna <Davis.Donna@epa.gov>
Subject: RE: Cumulative language for Conazoles - Conversation with Angela Huskey - Mefentrifluconazole

Angela-

Ex. 5 AC/DP

Please let me know if you have any questions.

Thanks,
Don

****
Donald Wilbur
Acting Associate Director
U.S. Environmental Protection Agency
Office of Pesticide Programs
Health Effects Division (7509P)
1200 Pennsylvania Ave NW
Washington, DC 20460
Telephone: (703)-347-8894
Email: Wilbur.Donald@epa.gov
****

From: Huskey, Angela
Sent: Monday, June 3, 2019 12:46 PM
To: Ertman, AWillis <Ertman.AWillis@epa.gov>; Perron, Monique <Perron.Monique@epa.gov>; Olinger, Christine <Olinger.Christine@epa.gov>
Cc: Godshall, Joshua <Godshall.Joshua@epa.gov>; Wilbur, Donald <Wilbur.Donald@epa.gov>; Fitz, Nancy <Fitz.Nancy@epa.gov>; Muhammad, Maryam K. <Muhammad.Maryam@epa.gov>; Davis, Kable <Davis.Kable@epa.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>
Subject: RE: Cumulative language for Conazoles - Conversation with Angela Huskey - Mefentrifluconazole

Sorry, with the attachment.

Angela Huskey | US EPA | Office of General Counsel | 1200 Pennsylvania Ave., NW | William Jefferson Clinton Federal Building (WJC), Mail Code 2333A | Washington DC 20460 | phone: (202) 564-2892

From: Huskey, Angela
Sent: Monday, June 03, 2019 12:45 PM
To: Ertman, AWillis <Ertman.AWillis@epa.gov>; Perron, Monique <Perron.Monique@epa.gov>; Olinger, Christine <Olinger.Christine@epa.gov>
Cc: Godshall, Joshua <Godshall.Joshua@epa.gov>; Wilbur, Donald <Wilbur.Donald@epa.gov>; Fitz, Nancy <Fitz.Nancy@epa.gov>; Muhammad, Maryam K. <Muhammad.Maryam@epa.gov>; Davis, Kable <Davis.Kable@epa.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>
Subject: RE: Cumulative language for Conazoles - Conversation with Angela Huskey - Mefentrifluconazole

Hi all,

Ex. 5 Deliberative Process (DP) / Attorney-Client

Thanks,
Angela

Angela Huskey | US EPA | Office of General Counsel | 1200 Pennsylvania Ave., NW | William Jefferson Clinton Federal Building (WJC), Mail Code 2333A | Washington DC 20460 | phone: (202) 564-2892

From: Ertman, AWillis
Sent: Wednesday, May 22, 2019 9:54 AM

To: Perron, Monique <Perron.Monique@epa.gov>; Olinger, Christine <Olinger.Christine@epa.gov>; Huskey, Angela <Huskey.Angela@epa.gov>
Cc: Godshall, Joshua <Godshall.Joshua@epa.gov>; Wilbur, Donald <Wilbur.Donald@epa.gov>; Fitz, Nancy <Fitz.Nancy@epa.gov>; Muhammad, Maryam K. <Muhammad.Maryam@epa.gov>; Davis, Kable <Davis.Kable@epa.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>
Subject: RE: Cumulative language for Conazoles - Conversation with Angela Huskey - Mefentrifluconazole

All,
Attached is the working copy with all changes incorporated and the cumulative language as approved by HED.

Angela,
Please confirm that this version is good to go and we'll send it on for typesetting.

Let me know if you have any questions.
Thanks, Andy

From: Perron, Monique
Sent: Wednesday, May 22, 2019 9:38 AM
To: Ertman, AWillis <Ertman.AWillis@epa.gov>; Olinger, Christine <Olinger.Christine@epa.gov>; Huskey, Angela <Huskey.Angela@epa.gov>
Cc: Godshall, Joshua <Godshall.Joshua@epa.gov>; Wilbur, Donald <Wilbur.Donald@epa.gov>; Fitz, Nancy <Fitz.Nancy@epa.gov>; Muhammad, Maryam K. <Muhammad.Maryam@epa.gov>; Davis, Kable <Davis.Kable@epa.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>
Subject: RE: Cumulative language for Conazoles - Conversation with Angela Huskey - Mefentrifluconazole

Yes, that is correct.

Thanks,
Monique

From: Ertman, AWillis
Sent: Wednesday, May 22, 2019 9:32 AM
To: Perron, Monique <Perron.Monique@epa.gov>; Olinger, Christine <Olinger.Christine@epa.gov>; Huskey, Angela <Huskey.Angela@epa.gov>
Cc: Godshall, Joshua <Godshall.Joshua@epa.gov>; Wilbur, Donald <Wilbur.Donald@epa.gov>; Fitz, Nancy <Fitz.Nancy@epa.gov>; Muhammad, Maryam K. <Muhammad.Maryam@epa.gov>; Davis, Kable <Davis.Kable@epa.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>
Subject: RE: Cumulative language for Conazoles - Conversation with Angela Huskey - Mefentrifluconazole

Ex. 5 Deliberative Process (DP)

Ex. 5 Deliberative Process (DP)

If this is okay with everyone, I think this is the last issue before sending this for typesetting.
Thanks, Andy

From: Perron, Monique
Sent: Wednesday, May 22, 2019 9:23 AM
To: Ertman, AWillis <Ertman.AWillis@epa.gov>; Olinger, Christine <Olinger.Christine@epa.gov>; Huskey, Angela <Huskey.Angela@epa.gov>
Cc: Godshall, Joshua <Godshall.Joshua@epa.gov>; Wilbur, Donald <Wilbur.Donald@epa.gov>; Fitz, Nancy <Fitz.Nancy@epa.gov>; Muhammad, Maryam K. <Muhammad.Maryam@epa.gov>; Davis, Kable <Davis.Kable@epa.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>
Subject: RE: Cumulative language for Conazoles - Conversation with Angela Huskey - Mefentrifluconazole

Andy,

Ex. 5 Deliberative Process (DP)

Thanks,
Monique

From: Ertman, AWillis
Sent: Wednesday, May 22, 2019 9:11 AM
To: Olinger, Christine <Olinger.Christine@epa.gov>; Huskey, Angela <Huskey.Angela@epa.gov>
Cc: Godshall, Joshua <Godshall.Joshua@epa.gov>; Wilbur, Donald <Wilbur.Donald@epa.gov>; Perron, Monique <Perron.Monique@epa.gov>; Fitz, Nancy <Fitz.Nancy@epa.gov>; Muhammad, Maryam K. <Muhammad.Maryam@epa.gov>; Davis, Kable <Davis.Kable@epa.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>
Subject: RE: Cumulative language for Conazoles - Conversation with Angela Huskey - Mefentrifluconazole

Hi Angela (and everyone else),

Ex. 5 Deliberative Process (DP)

Thanks, Andy

From: Olinger, Christine
Sent: Tuesday, May 21, 2019 3:00 PM
To: Huskey, Angela <Huskey.Angela@epa.gov>
Cc: Godshall, Joshua <Godshall.Joshua@epa.gov>; Ertman, AWillis <Ertman.AWillis@epa.gov>; Wilbur, Donald <Wilbur.Donald@epa.gov>; Perron, Monique <Perron.Monique@epa.gov>
Subject: FW: Cumulative language for Conazoles - Conversation with Angela Huskey - Mefentrifluconazole

Angela –
I spoke with Don about the conazole language and he has concerns about the detailed language that you are suggesting – please see his note below.

Chris Olinger

Christine Olinger
Chief, Risk Assessment Branch I
Office of Pesticide Programs Health Effects Division
US Environmental Protection Agency
1200 Pennsylvania Ave NW MailCode 7509P
Washington DC 20460
Office Location: Potomac Yard South Room 10751
Phone: 703-305-5406
FAX: 703-305-5147
olinger.christine@epa.gov

From: Wilbur, Donald
Sent: Tuesday, May 21, 2019 1:47 PM
To: Olinger, Christine <Olinger.Christine@epa.gov>; Vogel, Dana <Vogel.Dana@epa.gov>
Cc: Godshall, Joshua <Godshall.Joshua@epa.gov>; Perron, Monique <Perron.Monique@epa.gov>; Reaves, Elissa <Reaves.Elissa@epa.gov>
Subject: RE: Cumulative language for Conazoles - Conversation with Angela Huskey - Mefentrifluconazole

Folks-

Ex. 5 Deliberative Process (DP)

Thanks,
Don

****
Donald Wilbur
Acting Associate Director
U.S. Environmental Protection Agency
Office of Pesticide Programs
Health Effects Division (7509P)
1200 Pennsylvania Ave NW
Washington, DC 20460
Telephone: (703)-347-8894
Email: Wilbur.Donald@epa.gov
****

From: Olinger, Christine
Sent: Tuesday, May 21, 2019 12:26 PM
To: Wilbur, Donald <Wilbur.Donald@epa.gov>; Vogel, Dana <Vogel.Dana@epa.gov>
Cc: Godshall, Joshua <Godshall.Joshua@epa.gov>
Subject: Cumulative language for Conazoles - Conversation with Angela Huskey - Mefentrifluconazole

Don, Dana –

Ex. 5 Deliberative Process (DP)

Chris O.

Below is the language from the draft FR for mefentrifluconazole.

Ex. 5 Deliberative Process (DP)

Below is the cumulative section from the final mefentrifluconazole RA.
Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to mefentrifluconazole and any other substances. Although the conazole fungicides (triazoles) produce 1,2,4 triazole and its acid-conjugated metabolites (triazolylalanine and triazolylacetic acid), 1,2,4 triazole and its acid-conjugated metabolites do not contribute to the toxicity of the parent conazole fungicides (triazoles). The agency has assessed the aggregate risks from the 1,2,4 triazole and its acid-conjugated metabolites (triazolylalanine and triazolylacetic acid) separately. Mefentrifluconazole does not appear to produce any other toxic metabolite produced by other substances. For the purposes of this action, therefore, EPA has not assumed that mefentrifluconazole has a common mechanism of toxicity with other substances. In 2016, EPA's Office of Pesticide Programs released a guidance document entitled, *Pesticide Cumulative Risk Assessment: Framework for Screening Analysis* [https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/pesticide-cumulative-risk-assessment-framework]. This document provides guidance on how to screen groups of pesticides for cumulative evaluation using a two-step approach beginning with the evaluation of available toxicological information and if necessary, followed by a risk-based screening approach. This framework supplements the existing guidance documents for establishing common mechanism groups (CMGs)[1] and conducting cumulative risk assessments (CRA)[2]. During Registration Review, the Agency will utilize this framework to determine if the available toxicological data for mefentrifluconazole suggests a candidate CMG may be established with other pesticides. If a CMG is established, then a screening-level toxicology and exposure analysis may be conducted to provide an initial screen for multiple pesticide exposure.

Below is an FR for prothioconazole that went out last year and is the language she is quoting – see yellow highlights.
https://www.govinfo.gov/content/pkg/FR-2018-10-19/html/2018-22857.htm
Prothioconazole is a member of the conazole class of pesticides containing the 1,2,4-triazole moiety. Although conazoles act similarly in plants (fungi) by inhibiting ergosterol biosynthesis, there is not necessarily a relationship between their pesticidal activity and their mechanism of toxicity in mammals. Structural similarities do not constitute a common mechanism of toxicity. Evidence is needed to establish that the chemicals operate by the same, or essentially the same, sequence of major biochemical events in mammals (EPA, 2002). In the case of conazoles, however, a variable pattern of toxicological

[1] Guidance for Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity (USEPA, 1999)
[2] Guidance on Cumulative Risk Assessment of Pesticide Chemicals That Have a Common Mechanism of Toxicity (USEPA, 2002)

responses is found. Some are hepatotoxic and hepatocarcinogenic in mice. Some induce thyroid tumors in rats. Some induce developmental, reproductive, and neurological effects in rodents. Furthermore, the conazoles produce a diverse range of biochemical events including altered cholesterol levels, stress responses, and altered DNA methylation. It is not clearly understood whether these biochemical events are directly connected to their toxicological outcomes. Thus, there is currently no conclusive data to indicate that conazoles share common mechanisms of toxicity, and EPA is not following a cumulative risk approach for this the conazoles. For information regarding EPA's procedures for cumulating effects from substances found to have a common mechanism of toxicity, see EPA's website at http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/cumulative-assessment-risk-pesticides.

Prothioconazole is a triazole-derived pesticide. This class of compounds can form the common metabolite 1,2,4-triazole and two triazole conjugates (triazolylalanine and triazolylacetic acid). To support existing tolerances and to establish new tolerances for triazole-derivative pesticides, including prothioconazole, EPA conducted a human health risk assessment for exposure to 1,2,4-triazole, triazolylalanine, and triazolylacetic acid resulting from the use of all current and pending uses of any triazole-derived fungicide. The risk assessment is a highly conservative, screening-level evaluation in terms of hazards associated with common metabolites (e.g., use of a maximum combination of uncertainty factors) and potential dietary and non-dietary exposures (i.e., high end estimates of both dietary and non-dietary exposures). The Agency retained a 3X for the LOAEL to NOAEL safety factor when the reproduction study was used. In addition, the Agency retained a 10X for the lack of studies including a developmental neurotoxicity (DNT) study. The assessment includes evaluations of risks for various subgroups, including those comprised of infants and children. The Agency's complete risk assessment is found in the propiconazole reregistration docket at http://www.regulations.gov, Docket Identification (ID) Number EPA-HQ-OPP-2005-0497.

An updated dietary exposure and risk analysis for the common triazole metabolites 1,2,4-triazole (T), triazolylalanine (TA), triazolylacetic acid (TAA), and triazolylpyruvic acid (TP) was completed on July 18, 2017, in association with registration requests for the triazole fungicides difenoconazole and tetraconazole. That analysis concluded that risk estimates were below the Agency's level of concern for all population groups. The proposed new uses of prothioconazole are not expected to significantly increase the dietary exposure estimates for free triazole or conjugated triazoles; thus, the Agency is relying on the July 18, 2017 analysis to support its conclusion that the exposure to the triazole metabolite, including exposures from the use of prothioconazole on the commodities in subgroup 20A, does not present risks of concern. This assessment may be found on http://www.regulations.gov by searching for the following title and docket number: ``Common Triazole Metabolites: Updated Aggregate Human Health Risk Assessment to Address New Section 3 Registrations for Use of Difenoconazole and Tetraconazole.'' (located in docket ID number EPA-HQ-OPP-2016-0254).

Below is the cumulative language in the prothioconazole risk assessment from last year.

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to prothioconazole and any other substances. Although the conazoles produce 1,2,4 triazole and its acid-conjugated metabolites (triazolylalanine and triazolylacetic acid), 1,2,4 triazole and its acid-conjugated metabolites do not contribute to the toxicity of the parent conazoles. The Agency has assessed the aggregate risks from the 1,2,4 triazole and its acid-conjugated metabolites (triazolylalanine and triazolylacetic acid) separately. Prothioconazole does not appear to produce any other toxic metabolite produced by other substances. For the purposes of this action, therefore, EPA has not assumed that prothioconazole has a common mechanism of toxicity with other substances. In 2016, EPA's Office of Pesticide Programs released a guidance document

entitled, *Pesticide Cumulative Risk Assessment: Framework for Screening Analysis* [https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/pesticide-cumulative-risk-assessment-framework]. This document provides guidance on how to screen groups of pesticides for cumulative evaluation using a two-step approach beginning with the evaluation of available toxicological information and if necessary, followed by a risk-based screening approach. This framework supplements the existing guidance documents for establishing common mechanism groups (CMGs)[3] and conducting cumulative risk assessments (CRA)[4]. During Registration Review, the agency will utilize this framework to determine if the available toxicological data for prothioconazole suggests a candidate CMG may be established with other pesticides. If a CMG is established, a screening-level toxicology and exposure analysis may be conducted to provide an initial screen for multiple pesticide exposure.

[3] *Guidance For Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity* (USEPA, 1999)

[4] *Guidance on Cumulative Risk Assessment of Pesticide Chemicals That Have a Common Mechanism of Toxicity* (USEPA, 2002)